Volume 1 Issue 3 2012

ISSN: 2320- 480X

The Journal of Phytopharmacology

(Pharmacognosy and Phytomedicine Research)

Letter to Editor: Silymarin as potent Hepatoprotectants

Madhusudan Upadhyaya

A.S.R. Govt. Junior College, Khammameth-507001

Silymarin (Legalon®) isolated from the seeds of Silybum marianum (Asteraceae) is a mixture of flavolignans (1.5−3%, in fruits)− silybin, silidianin and silychristin (Figure 1). It has been studied in detail, and compared with all plant substances known to possess antihepatotoxic activity.[1]

The hepatoprotective activity of silymarin has been evaluated in various chemically-induced models of hepatotoxicity, including carbon tetrachloride, thioacetamide, galactosamine, thallium, lead and cadmium poisoning, and in a biological model of Plasmodium berghei infection in Mastomys.

The hepatotoxic effect of various substances is recognized mainly by the formation of free radicals through an activation process. Oxygen free radicals also play a significant role in hepatic intoxication through lipid peroxidation.

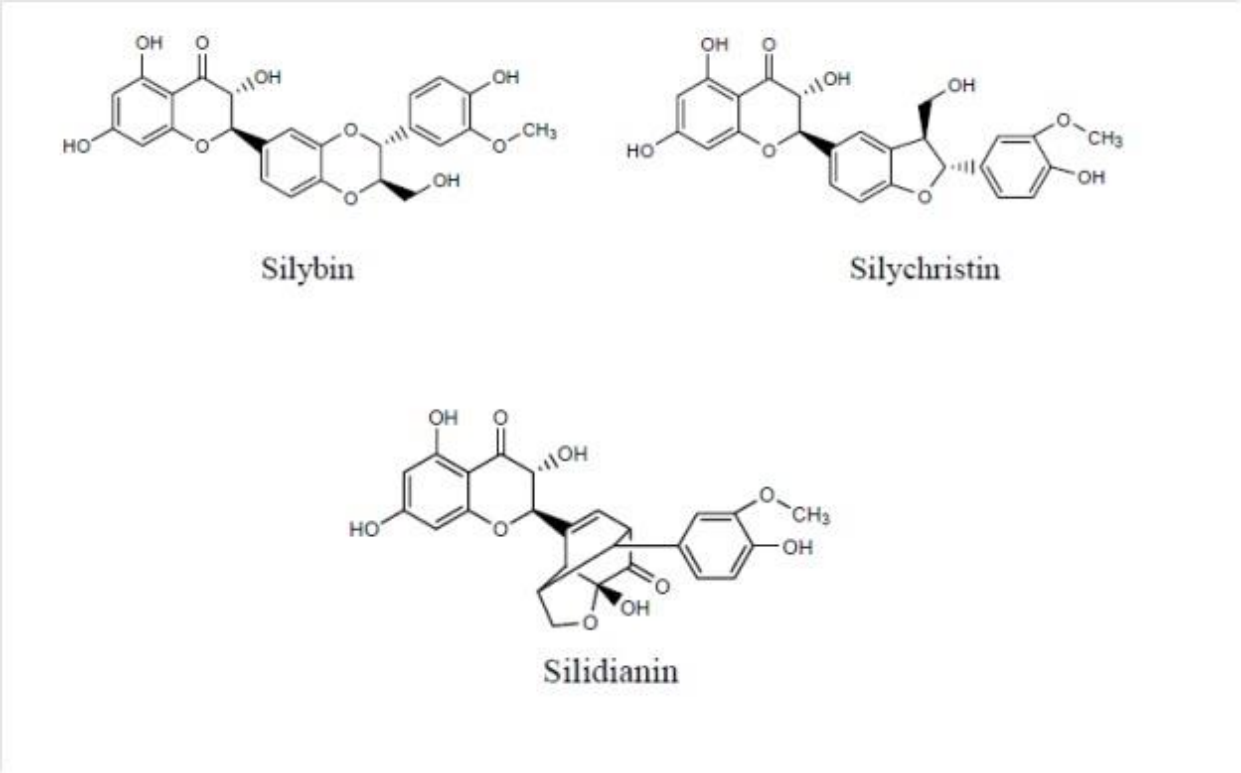

Figure: 1- Structure of Silybin, Silychristin and Silidianin

The two principal physiological defense systems involved against free radicals are the glutathione (GSH) and superoxide dismutase systems. In the case of an overload of toxic substances, the detoxification systems are deactivated due to exhaustion. Because of the phenolic nature, silymarin and its main constituent silybin display antioxidant properties and are able to react with numerous radicals in cell-free systems, including superoxide anion and hydroxide radicals. Thus, silybin inhibits superoxide anion radical O_2^- and NO in a dose-dependent manner, while it does not affect tumor necrosis factor-α (TNF-α) formation. It affects the metabolism of arachidonic acid by inhibiting cyclooxygenase and 5-lipoxygenase enzymes, but has no effect on prostaglandin E2 formation even at higher concentrations. Besides hepatoprotective activity, silybin also exhibits cytoprotective properties.[2]

In vivo studies using rats demonstrated that silybin stimulates RNA polymerase I and the synthesis of ribosomal RNA, increasing the pace of ribosome formation and thus also of protein synthesis. It also stimulates the synthesis of DNA in the hepatectomized rat and consequently the cell division and the regeneration of liver cells.

Four levels of action have been proposed for silymarin in experimental animals: 1) as an antioxidant by scavenging prooxidant free radicals and by increasing the intracellular concentration of GSH; 2) regulatory action of cellular membrane permeability and increase in its stability against xenobiotics injury; 3) increasing the synthesis of ribosomal RNA by stimulating DNA polymerase-I and by exerting a steroid like regulatory action on DNA transcription; and 4) stimulation of protein synthesis and regeneration of liver cells.[3]

On the basis of numerous pharmacological and toxicological studies, it is concluded that silymarin and its chief constituent, silybin, are highly effective and well tolerated. The principal target of its activity is the membrane of liver cells and of the organelles within the cytoplasm. This property, in combination with antioxidant and liver-regenerating properties, makes silymarin and its main constituent silybin therapeutically viable for the treatment of hepatic disorders of different origins. From the clinical point of view, silymarin is the best documented drug for the treatment of liver intoxication. Clinical studies of silymarin have demonstrated that its efficacy is not limited to the treatment of toxic and metabolic liver damage; silymarin is also effective in acute and chronic hepatitis. Moreover, it was shown to be highly effective in alcohol-induced hepatic disorders in a study that involved 200 patients. In the patients treated with 420 mg of silymarin/day for six months, the condition of the liver improved. In a double-blind, randomized study on 170 patients with cirrhosis of different etiologies and a multicenter, open study on 277 patients with chronic viral hepatitis, cirrhosis, fatty liver and other hepatopathies, scientists demonstrated the efficacy of silymarin in inhibiting fibrotic activity.[4]

Silymarin is poorly soluble in water, so an aqueous preparation made of fruit is ineffective. It is poorly absorbed in the gastrointestinal tract, and thus it is best administered parenterally. Oral use of

silymarin requires a concentrated product; it is marketed as a food supplement in the form of 200-mg capsules of concentrated extract, each capsule containing 140 mg of silymarin.

Mainly the seeds of the herb are used as an antihepatotoxic agent, in the form of tincture, capsule or tablets. A 5-ml dose of tincture improves function in chronic liver hepatitis and a dose of two to three capsules twice a day is recommended for successful treatment of hepatitis and liver cirrhosis.

The application of silybin is limited owing to poor bioavailability; however, different preparations of the drug have been created to increase its oral absorption, thereby enhancing its efficacy.[5]

Reference:

1. Morazzoni, P.; Bombardelli, E. Fitoterapia 1995, 66, 3−42.
2. Munday, R.; Winterbourn, C.C. Reduced glutathione in combination with superoxide dismutase as an important biological antioxidant defence mechanism Biochem. Pharmacol. 1989, 38, 4349−4357.
3. Sonnenbichler, J.; Goldsberg, M.; Hane, H. Biochem. Pharmacol. 1986, 5, 538−541.
4. Hikino, H.; Kiso, Y. Economic and Medicinal Plant Research, Academic Press: London, 1988; Vol. 2, pp 39.
5. Ferenci, P.; Dragosis, B.; Dittrich, H. J. Hepatol. 1989, 9, 105−113.